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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/593,950	05/10/2007	Wesley Blackaby	21573YP	5436

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EXAMINER	
RICCI, CRAIG D	
ART UNIT	PAPER NUMBER
1614	

MAIL DATE	DELIVERY MODE
12/23/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/593,950	BLACKABY ET AL.	
	Examiner	Art Unit	
	CRAIG RICCI	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 December 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-27* is/are pending in the application.

4a) Of the above claim(s) *9, 15-17,20- 21 and 24-27* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8,10-14,18,19,22 and 23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

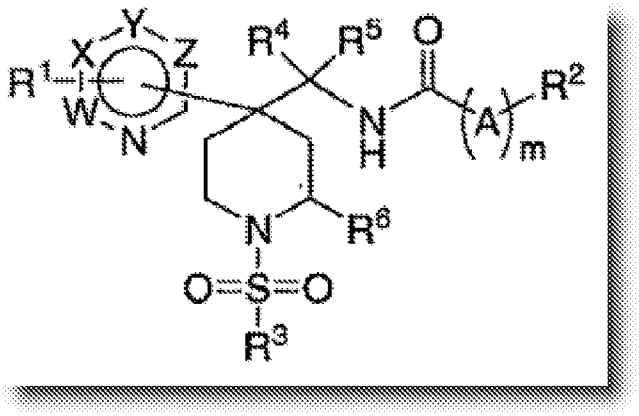
1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *9/22/2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

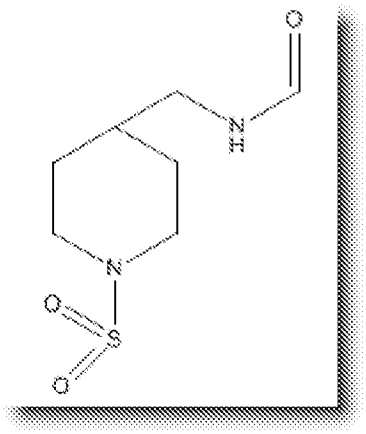
DETAILED ACTION

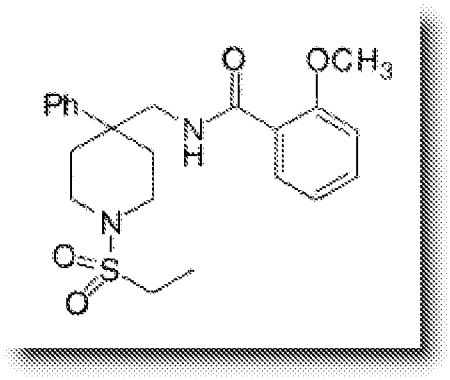
Status of the Claims

1. Claims 1-27 are currently pending. Claims 15-17, 21 and 24-27 are withdrawn. Additionally, claims 9 and 20 which are drawn to a non-elected species are withdrawn. Accordingly, claims 1-8, 10-14, 18-19 and 22-23 are the subject of this Office Action. This is the first Office Action on the merits of the claims.

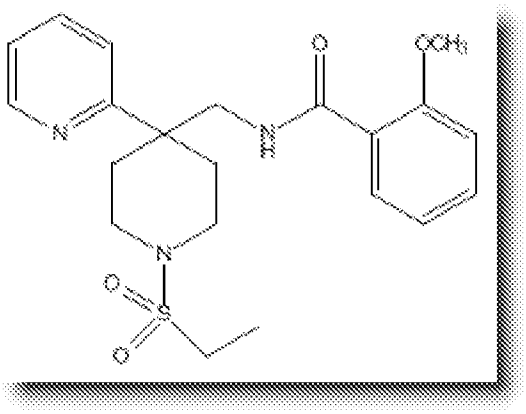
Election/Restrictions

2. Applicant's election with traverse of Group I in the reply filed on 12/16/2008 is acknowledged. Applicant traverses on the ground that the presently claimed compounds possess non-obvious structural differences as compared to the compounds of *Burnett*. Although Examiner agrees with Applicant, the restriction requirement is maintained in view of *Bao et al* (WO 2000/25786). Claim 1 is drawn to compounds of the generic formula (I):  wherein the variables are as defined by the claim. Notably, the variables encompass numerous possibilities, including the possibility that each variable is an additional variable that similarly encompass numerous possibilities. As such, the only feature shared by the millions of potential compounds of formula (I) is the following core:


. *Bao et al*, teach the following compound


which clearly contains the shared technical feature of the instant compounds of formula (I). As such, the technical feature of the instant compounds is not special. Furthermore, the restriction requirement is maintained in view of *Bao et al* in view of *Williams et al* (Foye's Principles of Medicinal Chemistry, 5th Ed., 2002) and *Patani et al* (Chem Rev 96:3147-3176, 1996) for the reasons discussed in detail below.

3. Claims 15-17, 21 and 24-27 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 12/16/2008.

4. Additionally, Applicant's election with traverse of Compound III-5 in the reply filed on 12/16/2008 is acknowledged. The elected species read upon claims 1-8, 11-14, 18-19 and 22-23. However, since the elected species was searched and is deemed free of the prior art, the search was therefore expanded as called for under current Office Markush Practice - a compound by compound search—to include a single additional species. That species is  wherein R^1 is hydrogen; R^2 is phenyl, which is substituted with R^{2a} and R^{2a} is O-CH_3; R^3 is CH_2-CH_3; R^4, R^5 and R^6 are hydrogen; W, X, Y and Z are C; and m is zero, which reads on claims 1-8, 10-14 and 18-19.

5. Claims 9 and 20 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected specie, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 12/16/2008.

Claim Rejections - 35 USC § 103

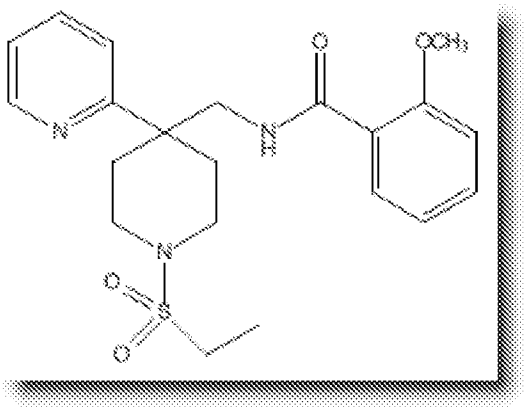
6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and

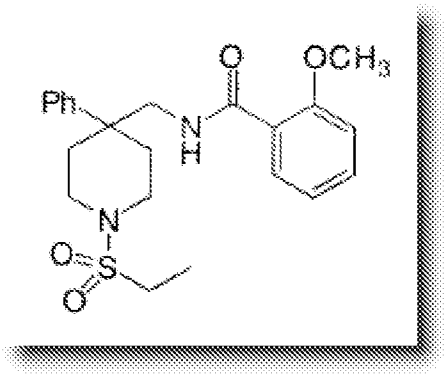
the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

8. **Claims 1-5, 10-14 and 23 are rejected under 35 U.S.C. 103(a) as being unpatentable over *Bao et al* (WO 2000/25786) as evidenced by *Rogers et al* (Brain Res, 493:41-50, 1989) in view of *Williams et al* (Foye's Principles of Medicinal Chemistry, 5th Ed., 2002) and *Patani et al* (Chem Rev 96:3147-3176, 1996)**.

9. Instant claim 1 is drawn to a compound of formula (I) which encompasses the following hypothetical compound  wherein R^1 is hydrogen; R^2 is phenyl, which is substituted with R^{2a} and R^{2a} is O-CH_3; R^3 is CH_2-CH_3;

R^4, R^5 and R^6 are hydrogen; W, X, Y and Z are C; and m is zero, and which reads on claims 1-5 and 10-14. Furthermore, the compounds of formula (I) are alleged to be useful in the treatment of neurological disorders associated with glutaminergic neurotransmission.

10. *Bao et al* teach the following compound 

(Page 61, Example 18) which is useful as potassium channel inhibitors for the treatment of a variety of disease conditions, including senile dementia, which is known to be associated with glutaminergic neurotransmission as evidenced by *Rogers et al* (abstract). Accordingly, *Bao et al* teach structurally and functionally related compounds differing only in the substitution of benzene (as taught by *Bao et al*) with pyridine as recited by the instant claims.

11. It would have been obvious to a person of ordinary skill in the art at the time the invention was made to replace benzene in the compounds taught by *Bao et al* with pyridine as claimed in the instant application for the following reason: as taught by *Williams et al* "When a lead compound is first discovered for a particular disease state, it often lacks the required potency and pharmacokinetic properties suitable for making it a viable clinical candidate… The medicinal chemist therefore must modify the compound

to reduce or eliminate these undesirable features without losing the desired biological activity. Replacement or modification of functional groups with other groups having similar properties is known as isosteric or bioisosteric replacement" (Page 59). Although it is clear that "the use of bioisosteric replacement (classical or nonclassical) in drug development is highly dependent upon the biological system being investigated" and that "No hard and fast rules exist to determine what bioisosteric replacement is going to work with a given molecule" it is also clear that "some generalizations have been possible" (Page 60). Notably, one such generalization is that -CH= and –N= (which are classic biosteric groups) can replace each other (Page 61, Table 2.9). Indeed, *Patani et al* similarly teach that benzene and pyridine are classic ring equivalent bioisosteres (Page 3158, Column 1). Accordingly, it would have been obvious to a person of ordinary skill in the art at the time the invention was made to replace the –CH= group in benzene (as taught by *Bao et al*) with –NH= to form pyridine (as recited by the instant claims). The person of ordinary skill in the art at the time the invention was made would have been motivated to make the bioisosteric modifications to synthesize similar compounds that retain biological activity, but have improved physiochemical properties and better pharmacokinetic behavior. As such, claims 1-8, 10-14 and 18-19 are rejected as *prima facie* obvious.

12. Instant claim 23 is drawn to a pharmaceutical composition which comprises a pharmaceutically acceptable carrier and a compound of claim 1 or salt thereof. *Bao et al* specifically disclose that "[a]lso within the scope of this invention are pharmaceutical

formulations comprising a compound of Formula I and a pharmaceutical carrier" (Page 9, Lines 13-15). Accordingly, claim 23 is rejected as *prima facie* obvious.

Double Patenting

13. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

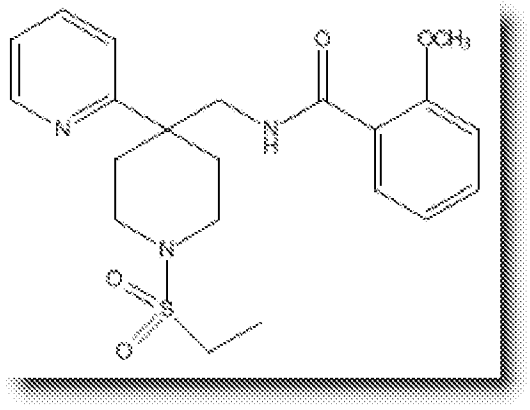
A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

14. **Claims 1-8, 10-14, 18-19 and 23 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 4 and 18 of copending Application No. 10/579,261 in view of *Williams et al* (Foye's Principles of Medicinal Chemistry, 5th Ed., 2002) and *Patani et al* (Chem Rev 96:3147-3176, 1996)**.

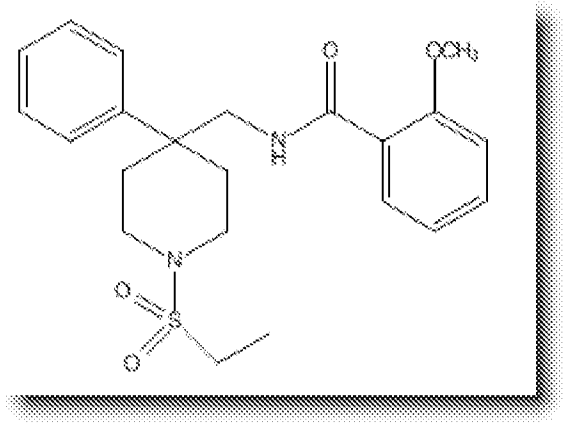
This is a provisional obviousness-type double patenting rejection.

15. As discussed above, instant claim 1 is drawn to a compound of formula (I) which encompasses the following hypothetical compound



wherein R^1 is hydrogen; R^2 is phenyl, which is substituted with R^{2a} and R^{2a} is O-CH_3; R^3 is CH_2-CH_3; R^4, R^5 and R^6 are hydrogen; W, X, Y and Z are C; and m is zero, and which reads on claims 1-8, 10-14 and 18-19.

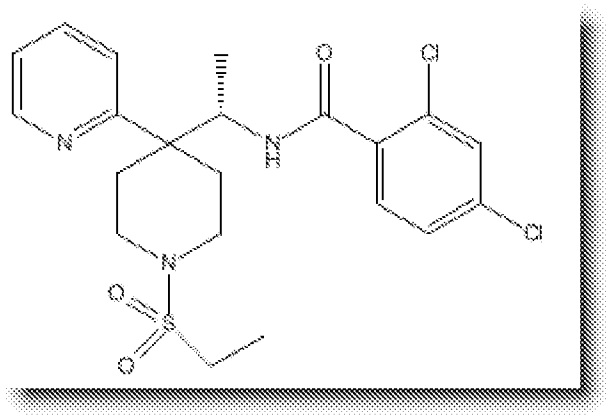
16. Claim 1 of the '261 application is drawn to a compound of formula (I) which encompasses the following hypothetical compound



wherein R^1 is hydrogen; R^2 is phenyl, which is substituted with O-CH_3; R^3 is CH_2-CH_3; and R^4 and R^5 are hydrogen. Accordingly, the '261 application teaches structurally and functionally related compounds differing only in the substitution of benzene (as taught by the '261 application) with pyridine as recited by the instant claims.

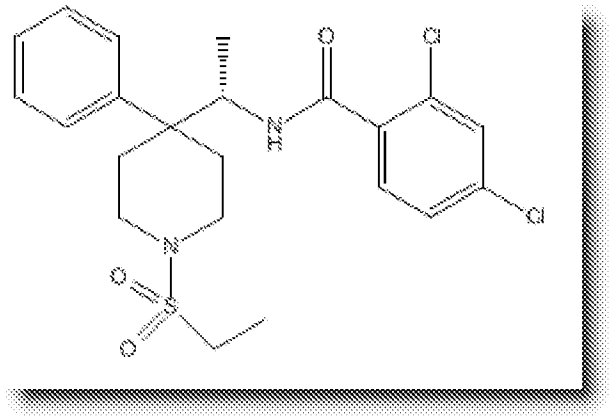
17. As discussed above, It would have been obvious to a person of ordinary skill in the art at the time the invention was made to replace benzene in the compounds taught the '261 application with pyridine as claimed in the instant application in view of *Williams et al* and *Patani et al*. The person of ordinary skill in the art at the time the invention was made would have been motivated to make the obvious bioisosteric modifications to synthesize similar compounds that retain biological activity, but have improved physiochemical properties and better pharmacokinetic behavior.

18. Instant claim 1 also encompasses Applicant's elected specie; namely



which reads on claims 1-8, 11-14, 18-19 and 22.

19. Claim 4 of the '261 application is drawn to a compound of formula (Ib) which encompasses the following hypothetical compound



wherein R^2 is phenyl, which is substituted with one or more halogens; and R^3 is CH_2-CH_3. Notably, the only difference between the instant elected compound specie and the above compound encompassed by claim 4 of the '261 application is the substitution of benzene (as taught by the '261 application) with pyridine as recited by the instant claims. Accordingly, for all of the

reasons discussed above, claims 1-8, 11-14, 18-19 and 22 (which are drawn to the instantly elected compound specie) are rejected.

20. Instant claim 23 is drawn to a pharmaceutical composition which comprises a pharmaceutically acceptable carrier and a compound of claim 1 or salt thereof. Claim 18 of the '261 application recites a pharmaceutical composition which comprises an inert carrier and a compound of Claim 1.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to CRAIG RICCI whose telephone number is (571) 270-5864. The examiner can normally be reached on Monday through Thursday, and every other Friday, 7:30 am - 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on (571) 272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/CRAIG RICCI/
Examiner, Art Unit 1614

/Ardin Marschel/
Supervisory Patent Examiner, Art Unit 1614